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10/018,200	01/23/2002	Lakshmi Archole Devi	5986/1F684-US1	4935

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EXAMINER

LANDSMAN, ROBERT S

ART UNIT

PAPER NUMBER

1647

10

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

10/018,200

Applicant(s)

DEVI ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 June 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 24-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☒ Claim(s) 1-23 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### ***1. Formal Matters***

A. Claims 1-35 are pending and were subject to restriction in Paper No. 7, dated 4/25/03. In Paper No. 9, filed 6/6/03, Applicants elected Group I with traverse. Applicants argue that Groups I-X should be examined together since they are not independent and distinct inventions, but rather species. However, these inventions are distinct since the field of search is different. A search for opioid-opioid receptor chimeras would not necessarily overlap a search of heteromeric opioid receptors which are fused to non-opioid receptors. Different key words would be required to search these independent inventions and to search every combination of chimeric receptors, e.g. mu-adrenergic, mu-delta opioid, mu, kappa opioid, mu-dopamine, mu-chemokine, delta-adrenergic, etc., would be an undue burden. However, the Examiner has decided to combine Groups I-X, claims 1-23, in full. The recitation of "in part" simply referred to the fact that certain claims were included in different Groups since they encompassed numerous independent and distinct inventions. However, this point is now moot.

B. The Information Disclosure Statement, filed 3/20/02, has been entered into the record.

### ***2. Claim Objections***

A. The syntax of claims 1, 11 and 19 could be improved by replacing the phrase "which receptor comprises" with "wherein said receptor comprises." Claims 2-10, 12, 13-18 and 20-23 are also objected to since they depend from objected base claims.

### ***3. Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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- A. Claims 1-23 are confusing since it is not clear whether the claimed dimers are a fusion protein or cross-linked.
- B. Claims 1-23 are confusing. Claims 1, 11 and 19 recite "receptor subunit." However, it is not clear what is meant by the term "subunit." The claims appear to encompass chimeras of entire opioid receptors, not subunits of receptors. It appears that the term "subunit" should be removed from the claims. Claims 2-10, 12, 16-18 and 20-23 are also rejected since they depend from rejected base claims.
- C. Claims 1-10 are confusing since it is not clear how the heterodimer can be "isolated" when both receptor subunits are expressed endogenously in the same cell.
- D. Claims 2-23 recite the limitation "receptor." There is insufficient antecedent basis for this limitation in the claim. Independent claims 1, 11 and 19 recite "receptor subunit" not solely a "receptor."
- E. Claims 11-18 are confusing since it is not clear how it is known that the receptors will form heterodimers simply by transfecting receptors encoded by individual expression vectors into a cell. If forming heterodimers were an inherent property of opioid receptors, then it is not clear how this would be distinct from the prior art, unless the claims are amended to recite that the host cell does not endogenously express multiple opioid receptor types.
- F. Claims 19-23 are confusing since it is not clear what novel feature is being performed in claim 19, since the only limitation is that opioid receptors are endogenously expressed in a cell. There is no "advantage" over the prior art, as will be seen below. It is also not clear how Applicants know that the method is being performed on a heterodimer as opposed to one or the other opioid receptor in a cell.

**4. Claim Rejections - 35 USC § 112, first paragraph – lack of enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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A. Claim 1, 5, 7, 9, 10-12, 15, 17 and 19-23 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for opioid-opioid, opioid-dopamine and opioid-adrenergic receptor dimers, does not reasonably provide enablement for opioid-chemokine dimmers, or any other opioid dimer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all dimers other than opioid-opioid, opioid-dopamine or opioid-adrenergic receptor dimers. Applicants provide no guidance or working examples of dimers other than opioid-opioid, opioid-dopamine and opioid-adrenergic receptor dimers. Furthermore, it is not predictable to one of ordinary skill in the art which receptors, other than those exemplified in the specification, form dimers with opioid receptors.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all opioid heterodimers. There is also a lack of guidance and working examples of these dimers other than opioid-opioid, opioid-dopamine and opioid-adrenergic receptor dimers. These factors, along with the lack of predictability to one of ordinary skill in the art as to which receptors would dimerize with opioid receptors, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

### **5. Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 19 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Knapp et al. (reference 1 on the IDS submitted 12/14/01). The claims recite a method of screening compounds which modulate an endogenous opioid heterodimer. Knapp et al. teach that the mu, delta and kappa opioid receptors are found in rat brain (page 518, entire right column through the first full paragraph of page

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519). Knapp et al. also teach that these receptors work via the adenylyl cyclase signal transduction pathway (Abstract). Knapp et al. also teach that various compounds have been screened which have binding affinity for these receptors (page 520 under "The Pharmacology of Cloned Opioid Receptors). Since the claims of the present invention do not recite that the cells have been transfected into a cell line which does not normally express opioid receptors, but that the cell endogenously expresses these receptors, Knapp et al. meet the limitation of the claims since the artisan, in screening rat brain, or any other mammalian brain, would inherently be practicing the present invention.

#### **6. Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. in view of Cvejic et al. (reference 3 on the IDS submitted 12/14/01). The teachings of Knapp et al. are seen in the above rejection under 35 USC 102. Knapp et al. do not teach the trafficking of dimers. However, Cvejic teach that the delta opioid receptor dimerizes (Abstract) and that these receptors internalize (i.e. trafficking – see Introduction). Therefore, it would have been obvious to the artisan at the time of the invention to have used an assay which measures receptor trafficking (i.e. internalization) since this was a well known property of delta opioid receptors and, therefore, the artisan would have had a reasonable expectation of success in measuring the internalization of an opioid dimer, including those of the invention. It would have been obvious for one of ordinary skill in the art at the time of the present invention to have performed this method especially in light of the teachings of Egan et al (Science 214) since Egan teach that both mu and delta opioid receptors exist endogenously in the same cell (Abstract).

#### **7. Conclusion**

A. No claim is allowable.

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***Advisory information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.  
Patent Examiner  
Group 1600  
August 06, 2003

  
**ROBERT LANDSMAN**  
**PATENT EXAMINER**